Citation:

Dickinson KM, Keogh JB, Clifton PM. Effects of a low-salt diet on flow-mediated dilatation in humans. *Am J Clin Nutr.* 2009 Feb; 89 (2): 485-490.

PubMed ID: 19106240

Study Design:

Randomized crossover trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the effects of a low-salt diet with those of a usual salt diet on flow-mediated dilatation in a weight-stable setting, and secondarily, to determine the effect of a low-salt diet on other measures of vascular function, namely aortic pulse wave velocity and augmentation index.

Inclusion Criteria:

None.

Exclusion Criteria:

Subjects who had one or more of the following:

- Metabolic disease
- Cardiovascular disease
- Systolic blood pressure greater than 160mmhg
- Significant weight loss in the preceding six months (more than 2kg)
- Body Mass Index less than 27 or greater than 40kg/m^2
- Using anti-hypertensive medication.

Description of Study Protocol:

Recruitment

Men and women were recruited from the Commonwealth Scientific and Industrial Research Organization volunteer database and screened for eligibility.

Design

Randomized crossover trial with two two-week dietary interventions.

Dietary Intake/Dietary Assessment Methodology

Three-day weighed food records were completed by subjects and analyzed.

Blinding Used

- Subjects were not blinded to interventions
- The operator who performed the flow-mediated dilatation measurements was unaware of the diet assignment at the time of the test.

Intervention

- Subjects were randomly assigned to either a usual salt or a low-salt diet and then crossed over to the other diet after two weeks. Both diets were designed to ensure weight stability. The background diet was designed to keep total saturated fat and potassium constant across both diet periods. Before each intervention, subjects were advised by a trained dietician on how to achieve either a low-salt or a usual salt diet and to keep their weight stable. The only study foods provided were salt-free bread and butter and salted bread and butter. Subjects were asked to keep alcohol intake and physical activity constant during the study.
    - Low-salt diet: 50mmol per day
    - Usual salt diet: 150mmol per day.

Statistical Analysis

- Analysis of variance with repeated measures was used (with diet as the within-subject factor) with and without covariates, including diet order, blood pressure, and baseline sodium excretion
- Pearson correlation analyses were conducted to assess the association of change between variables.

Data Collection Summary:

Timing of Measurements

- Three-day food records were collected each week of the study
- Body height and weight were measured at baseline
- Blood pressure, low-mediated dilatation, aortic pulse wave velocity and augmentation index measurements were measured after each dietary intervention
- A 24-hour urine sample was collected at baseline and at the end of each intervention to measure sodium and potassium.

Dependent Variables

- Brachial artery flow mediated dilatation: Measured in the morning after an overnight fast with a 7.5MHz linear array transducer
- Pulse wave velocity: Measured with Doppler recordings at the carotid and femoral arteries
- Augmentation index: Measured using the SphygmoCor blood pressure analysis system
- Blood pressure: Measured with an automated sphygmomanometer.

Independent Variables

- Low-salt diet: 50mmol per day
- Usual salt diet: 150mmol per day.

Control Variables

Weight loss, change in systolic and diastolic blood pressure and saturated fat intake.

Description of Actual Data Sample:

- *Initial N:* 32
- *Attrition (final N):* 29 (seven males, 22 females)
- *Age:* Mean (SD) was 52.7 (6.0) years
- *Ethnicity:* Not reported
- *Other relevant demographics:* None
- *Anthropometrics:* Mean (SD) for Body Mass Index was 31.6 (2.8)kg/m^2
- *Location:* Australia.

Summary of Results:

Measures of Vascular Function, Blood Pressure and Dietary Compliance at the End of Each Two-week Dietary Intervention (N=29).

Variables	Low-salt Diet Mean (SD)	Usual Salt Diet Mean (SD)	P-value (Repeated Measures ANOVA)
Baseline brachial artery diameter (mm)	4.14 (0.85)	4.10 (0.78)	P>0.05
Post-release brachial artery diameter (mm)	4.33 (0.85)	4.23 (0.77)	P>0.05
Flow mediated dilation (percentage)	4.89 (2.42)	3.37 (2.10)	P<0.01
Systolic blood pressure (mmHg)	112 (11)	117 (13)	P<0.05
Diastolic blood pressure (mmHg)	72 (8)	73 (7)	P>0.05
Mean arterial pressure (mmHg)	86 (9)	88 (8)	P>0.05
Pulse wave velocity (m/s)	10.49 (4.14)	10.49 (3.07)	P>0.05
Augmentation index (percentage)	27.49 (9.02)	28.06 (10.19)	P>0.05

Other Findings

- Compliance with the protocol was confirmed by 24-hour urinalysis. Sodium excretion was was significantly lower with the low-salt diet compared to the usual diet (P<0.001)
- Absolute low mediated dilatation was 1.52% greater with the low-salt diet than with the usual salt diet (an increase of about 30%). This change in flow mediated dilatation remained significant after controlling for weight loss, change in systolic and diastolic blood pressure, and saturated fat intake between the two treatments
- A small significant reduction in systolic blood pressure was observed after sodium reduction (P=0.02).

Author Conclusion:

- A sodium-restricted diet improved endothelial function, assessed by flow-mediated dilatation, relative to a usual salt diet in overweight and obese subjects
- In addition, change in flow mediated dilatation was unrelated to changes in blood pressure, which suggests that a mechanism other than change in blood pressure is responsible for the effect of salt on flow-mediated dilatation.

Reviewer Comments:

- *Author-identified limitations include the short duration of the intervention, the failure to measure NO metabolites, ADMA, cortisol, or GTN response and failure to measure the usual salt diet at baseline to assess differences between intervention and pre-study intakes*
- *More robust measures of flow mediated dilatation and blood pressure (e.g., 24-hour blood pressure monitoring) would have been useful to reduce variability*
- *A 24-hour urine collection may not have been adequate to characterized urinary sodium excretion.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	???
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes

4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes

7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	???
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	No
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	No
8.7.	If negative findings, was a power calculation reported to address type 2 error?	Yes
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes